



*A2
cont*

wherein:

R₁ is hydrogen, hydroxy, C₁-C₈ alkyl, C₁-C₈ alkoxy, halo, trifluoromethyl, or CN;

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R₂ is hydrogen ;

R₃, R₄, and R₅ independently are hydrogen, hydroxy, halo, trifluoromethyl, C₁-C₈ alkyl, C₁-C₈ alkoxy, nitro, CN, or -(O or NH)_m-(CH₂)_n-R₉, where R₉ is hydrogen, hydroxy, COOH, or NR₁₀R₁₁;

n is 0-4;

m is 0 or 1;

R₁₀ and R₁₁ independently are hydrogen or C₁-C₈ alkyl, or taken together with the nitrogen to which they are attached can complete a 3-10 member cyclic ring optionally containing 1, 2, or 3 additional heteroatoms selected from O, S, NH, or N-C₁-C₈ alkyl;

Z is COOR₇, tetrazolyl, CONR₆R₇, CONHNR₁₀R₁₁, or CH₂OR₇;

R₆ and R₇ independently are hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, (CO)-C₁-C₈ alkyl, aryl, heteroaryl, or C₃-C₁₀ cycloalkyl optionally containing one, two, or three heteroatoms selected from O, S, NH, or N alkyl; or R₆ and R₇ together with the nitrogen to which they are attached complete a 3-10 member cyclic ring optionally containing 1,2, or 3 additional heteroatoms selected from O, S, NH, or N alkyl; and wherein any of the foregoing alkyl, alkenyl, aryl, heterocyclic, and alkynyl groups can be unsubstituted or substituted by halo, hydroxy, C₁-

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Sub B 1
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C₆ alkoxy, amino, nitro, C₁-C₄ alkylamino, di(C₁-C₄) alkylamino, C₃-C₆ cycloalkyl, phenyl, phenoxy, C₃-C₅ heteroaryl, or C₃-C₅ heteroaryloxy;

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

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8. (Once Amended) The method of claim 6, wherein the MEK inhibitor is a compound of Formula (I) wherein (a) R₁ is hydrogen, methyl, methoxy, fluoro, chloro, or bromo; (b) R₂ is hydrogen; (c) R₃, R₄, and R₅ independently are hydrogen, fluoro, chloro, bromo, iodo, methyl, methoxy, or nitro; (d) R₁₀ and R₁₁ independently are hydrogen or methyl; (e) Z is COOR₇, tetrazolyl, CONR₆R₇, CONHNR₁₀R₁₁, or CH₂OR₇; R₆ and R₇ independently are hydrogen, C₁₋₄ alkyl, heteroaryl, or C₃₋₅ cycloalkyl optionally containing one or two heteroatoms selected from O, S, or NH; or R₆ and R₇ together with the nitrogen to which they are attached complete a 5-6 member cyclic ring optionally containing 1 or 2 additional heteroatoms selected from O, NH or N-alkyl; and wherein any of the foregoing alkyl or aryl groups can be unsubstituted or substituted by halo, hydroxy, methoxy, ethoxy, or heteroaryloxy.

A 4

14. (Once Amended) The method of claim 1, comprising a MEK inhibitor having a structure selected from:

2- (2-chloro-4-iodophenylamino)-5-chloro-N-cyclopropylmethoxy-3,4-difluorobenzamide;

2- (4-iodophenylamino)-N- cyclopropylmethoxy-5-chloro-3,4-difluorobenzamide;

2- (4- iodophenylamino)-5-chloro-3,4-difluorobenzoic acid;

2- (2- chloro-4-iodophenylamino)-5-chloro-3,4-difluorobenzoic acid;

5-chloro-3,4-difluoro-2- (4-ido-2-methylphenylamino)- benzoic acid; and

5-chloro-N-cyclopropylmethoxy-3,4- difluoro-2- (4-ido-2-methylphenylamino)-benzamide.

15. (Once Amended) A method of treating or preventing arthritis in a patient in need of treatment, or suspected of developing arthritis, said method comprising the

step of administering an effective antiarthritic amount of a compound selected from:

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2- (2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluorobenzamide;

2- (2-Methyl-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide;

2- (2-Methyl-4-iodophenylamino)-N-hydroxy-3,4-difluoro- 5-bromobenzamide;

2- (2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluoro-5-bromobenzamide;

2- (2-Methyl-4-iodophenylamino)-N-cyclobutylmethoxy- 3,4-difluoro-5-bromobenzamide;

2- (2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluoro-5-bromobenzamide;

2- (2-Chloro-4-iodophenylamino)-N-hydroxy-3,4-difluoro- 5-bromobenzamide;

2- (2-Chloro-4-iodophenylamino)-N-cyclobutylmethoxy- 3,4-difluorobenzamide;

2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide;

2- (2-Methyl-4-iodophenylamino)-N-hydroxy- 3,4-difluorobenzamide;

2- (2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4,5-trifluorobenzamide; and

2- (2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 4-fluorobenzamide.

16. (Once Amended) The method of Claim 15 wherein said compound is selected from

2- (2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluorobenzamide;

2- (2-Methyl-4-iodophenylamino)-N- cyclopropylmethoxy-3,4,5-trifluorobenzamide; and

2- (2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 4-fluorobenzamide.

Please add following new Claims 17, 18, and 19 as follows:

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17. (New) A method of treating or preventing arthritis in a patient in need of treatment, or suspected of developing arthritis, said method comprising the step of administering an effective antiarthritic amount of 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluorobenzamide.
18. (New) The method of Claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR₇; R₇ is H, pentafluorophenyl, or tetrazolyl; and R₃, R₄, and R₅ are independently H, fluoro, or chloro.
19. (New) The method of Claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR₇; R₇ is H, pentafluorophenyl, or tetrazolyl; and R₃, R₄, and R₅ independently are fluoro.